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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,143	11/26/2001	Brian L. Craine	4969-A-07	8603

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CAHILL, SUTTON & THOMAS P.L.C.
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EXAMINER

GAKH, YELENA G

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/994,143

Applicant(s)

CRAINE, BRIAN L.

Examiner

Yelena G. Gakh, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 25-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 112601.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Election filed 10/14/03 is acknowledged. Claims 1-~~24~~ are pending in the application. Claims 25-29 are withdrawn from the consideration.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 5 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for determining the location of bleeding when there are reference absorption spectra with known spectral ranges for different types of blood analytes related to upper and lower site bleeding, does not reasonably provide enablement for the method, when such reference spectra are absent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. No one of ordinary skill in the art can determine, whether blood came from an upper or lower GI site on the basis of absorption spectra, if no preliminary data on which absorption peaks can be observed for both cases exist.

Claims 2-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the conditions recited in claim 13, does not reasonably provide enablement for other conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. It is well known from the extensive literature that the absorption lines of various haemoglobins and derivatives depend on pH of their solutions, and therefore while the peaks of hemoglobin are observed at 540 and 576 nm when pH 7.4, different absorption peaks will be observed for other pH values, see e.g. Ingberg et al. (US 5,008,388): "in the albumin, the absorption spectrum is again very similar to that of hemoglobin with a high

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Soret maximum at 402 nm and the maxima in the visible at 510, 540, and 620 nm, typical for a high-spin ferric hemoprotein. In aqueous alcohol, the intensity of the Soret band has decreased and the maximum has shifted to 393 nm, whereas the visible spectrum is more diffused with maxima at 490 and 602 nm. In 0.9% sodium chloride, the Soret maximum has decreased further and is shifted to 390 nm, while the spectrum in visible wave lengths shows only a broad band at 600 nm" (col. 6, lines 40-64).

4. Claims 23-24 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Specific IR wavelengths for detecting ferriheme and ferroheme in specific conditions critical or essential to the practice of the invention, but not included in the claim(s) are not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The specification does not disclose any possible IR wavelength range for detecting ferriheme and ferroheme, which may significantly vary depending on conditions.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. **Claims 1 and 5** are rejected under 35 U.S.C. 103(a) as being unpatentable over Fielder et al. (US 5,460,969) with evidence of Benezra et al. (US 4,853,338) in view of Hacker (Arch. Verdauungs-Krankh., 1935, Abstract).

Fielder teaches a method for differentiating between locations of GI bleeding (upper or lower) based on detection of hemoglobin in a filtered and centrifuged stool sample, with the presence of hemoglobin indicating lower location of GI bleeding (Abstract), while “detection of hematin [a **ferric** heme derivative (Merck Index, 9th edition, see Benezra, col. 5, lines 56-57), with hemoglobin being **ferroheme**] in the stool will signify upper GI blood loss” (col. 2, ll.1-2).

Fielder does not specifically disclose spectroscopic measurement of the samples.

Hacker teaches “detection of occult bleeding in the gastrointestinal tract with special reference to the appearance of copratoporphyrin and hemoglobin” (Title), comprising spectroscopic examination of hemoglobin degradation products in feces, such as hematin and “copratoporphyrin”.

It would have been obvious for anyone of ordinary skill in the art to apply spectroscopic approach taught by Hacker in Fielder’s method of differentiating between locations of GI bleeding, because both Fielder and Hacker consider presence of unchanged hemoglobin (ferrous heme) in a stool sample as an indication of lower GI bleeding and the presence of hematin (ferric heme) as a sign for upper GI bleeding, with spectrometric approach being simpler and more straightforward. It would have been obvious for anyone of ordinary skill to use a reference sample without the stool sample for calibrating spectrometer and correcting for the background noise.

9. **Claims 2-4 and 6-8** are rejected under 35 U.S.C. 103(a) as being unpatentable over Fielder with evidence of Benezra in view of Hacker, as applied to claim 1 above, and further in view of Brady et al. (JBC, 1975).

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Fielder and Hacker in the Abstract do not specifically teach absorption peaks at 540 nm, 576 nm, 415 nm and 408 nm.

Brady discloses ferroheme and ferriheme spectroscopic parameters with absorption of ferroheme at 415 nm, 540 nm and 570 nm, and Soret absorbance of ferriheme at 407 nm.

It would have been obvious for anyone of ordinary skill in the art to detect the presence or absence of peaks at 540 nm, 576 nm and 415 nm, and for Soret line at 407-408 nm, disclosed by Brady, in Fielder-Hacker method, because the first set of absorptions is characteristic for hemoglobin, while Soret line at 408-409 nm is characteristic for hematin.

10. **Claims 9, 14-15 and 20-21** are rejected under 35 U.S.C. 103(a) as being unpatentable over Fielder with evidence of Benezra in view of Hacker and Machida et al. (US 5,759,866).

Fielder teaches a method for differentiating between locations of GI bleeding (upper or lower) based on detection of hemoglobin in a filtered and centrifuged stool sample, with the presence of hemoglobin indicating lower location of GI bleeding (Abstract), while “detection of hematin [a **ferric** heme derivative (Merck Index, 9th edition, see Benezra, col. 5, lines 56-57), with hemoglobin being **ferroheme**] in the stool will signify upper GI blood loss” (col. 2, ll.1-2).

Fielder does not specifically disclose spectroscopic measurement of the samples.

Hacker teaches “detection of occult bleeding in the gastrointestinal tract with special reference to the appearance of copratoporphyrin and hemoglobin” (Title), comprising spectroscopic examination of hemoglobin degradation products in feces, such as hematin and “copratoporphyrin”.

Fielder and Hacker do not particularly disclose nitrocellulose filter.

Machida indicates in the “Background of the Invention” a conventional use of nitrocellulose filter for the examination of fecal occult blood” (col. 1, lines 41-45).

It would have been obvious for anyone of ordinary skill in the art to apply spectroscopic approach taught by Hacker in Fielder’s method of differentiating between locations of GI bleeding, because both Fielder and Hacker consider presence of unchanged hemoglobin (ferrous heme) in a stool sample as an indication of lower GI bleeding and the presence of hematin (ferric heme) as a sign for upper GI bleeding, with spectrometric approach being simpler and more straightforward. It would have been obvious for anyone of ordinary skill to use a reference sample without the stool sample for calibrating spectrometer and correcting for the background

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noise. It would have been obvious to use nitrocellulose filter, because Machida indicates its conventional usage for analysis of biological samples. It would have been obvious to use either fecal extracts or deposit on the filter for spectrometric analysis, because both ways are conventional for this type of analysis and purify the samples using conventional biochemical separation methods.

11. **Claims 10-12 and 22** are rejected under 35 U.S.C. 103(a) as being unpatentable over Fielder with evidence of Benezra in view of Hacker and Machida, as applied to claims 9, 14-15 and 20-21 above, and further in view of Brady et al. (JBC, 1975).

Fielder in view of Hacker and Machida do not specifically teach absorption peaks at 540 nm, 576 nm, 415 nm and 408 nm.

Brady discloses ferroheme and ferriheme spectroscopic parameters with absorption of ferroheme at 415 nm, 540 nm and 570 nm, and Soret absorbance of ferriheme at 407 nm.

It would have been obvious for anyone of ordinary skill in the art to detect the presence or absence of peaks at 540 nm, 576 nm and 415 nm, and for Soret line at 407-408 nm, disclosed by Brady, in Fielder-Hacker-Machida's method, because the first set of absorptions is characteristic for hemoglobin, while Soret line at 408-409 nm is characteristic for hematin.

12. **Claim 13** is rejected under 35 U.S.C. 103(a) as being unpatentable over Fielder with evidence of Benezra in view of Hacker and Machida, as applied to claims 9, 14-15 and 20-21 above, and further in view of Schmitz (US 4,347,311).

Fielder, Benezra, Hacker and Machida do not disclose TE-buffer recited in claim 13; however Benezra teaches detecting hemoglobin at 540 nm and 576 nm in phosphate buffer at pH 7.5.

Schmitz discloses TE-buffer recited in claim 13 with pH 7.4 used for separating biological samples.

It would have been obvious to use TE-buffer with pH 7.4, disclosed by Schmitz for extracting biological samples, in Fielder-Hacker-Brady-Machida's method, because Benezra teaches detecting hemoglobin at pH 7.4 as the closest biological conditions.

13. **Claim 16** is rejected under 35 U.S.C. 103(a) as being unpatentable over Fielder with evidence of Benezra in view of Hacker and Machida, as applied to claims 9, 14-15 and 20-21 above, and further in view of HYDROFLUORTM-Combo.

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While Fielder in view of Hacker and Machida do not particularly disclose applying glycerol to the filter, HYDROFLUORTM-Combo discloses applying glycerol to the cellulose filter to make it transparent for the spectroscopic studies of the biological sample on the filter. It would have been obvious for anyone of ordinary skill in the art to apply glycerol to the nitrocellulose filter for the same reasons as indicated in HYDROFLUORTM-Combo, i.e. to make it transparent for spectrometric analysis.

14. **Claims 16-19** are rejected under 35 U.S.C. 103(a) as being unpatentable over Fielder with evidence of Benezra in view of Hacker and Machida, as applied to claims 9,14-15 and 20-21 above, and further in view of "Manual for Biochem 651" and well-known mathematical algorithms for treating complex spectra.

Fielder, Benezra, Hacker and Machida do not specifically disclose the ways of treating complex absorption spectra of heme-derivatives in different states using various mathematical algorithms.

Manual for Biochem 651 provide a simplified approach for treating such spectra for complex mixtures of heme in different states. It would have been obvious for anyone of ordinary skill in the art to apply well-known mathematical algorithms to treating complex absorption spectra of hemoglobin in different states, similar to what is provided in the Manual, using more sophisticated mathematical models, such as neural network, Simplex, or Gaussian Jordan elimination algorithm, because such models are well-known for using in treating complex absorption spectra, as admitted by the Applicants (Specification, page 20, lines 10-13).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (703) 306-5906. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

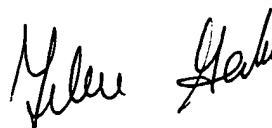
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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Yelena G. Gakh
12/8/03

A handwritten signature in black ink, appearing to read 'Yelena Gakh', written in a cursive style.